



Porphyria

By

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INTENDED LEARNING OBJECTIVES (ILOs)



By the end of this lecture the student will be able to:

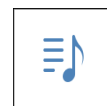
- 1. Outline different types of Porphyria**
- 2. Correlate biochemical basis of porphyria with its clinical manifestations**



Outlines

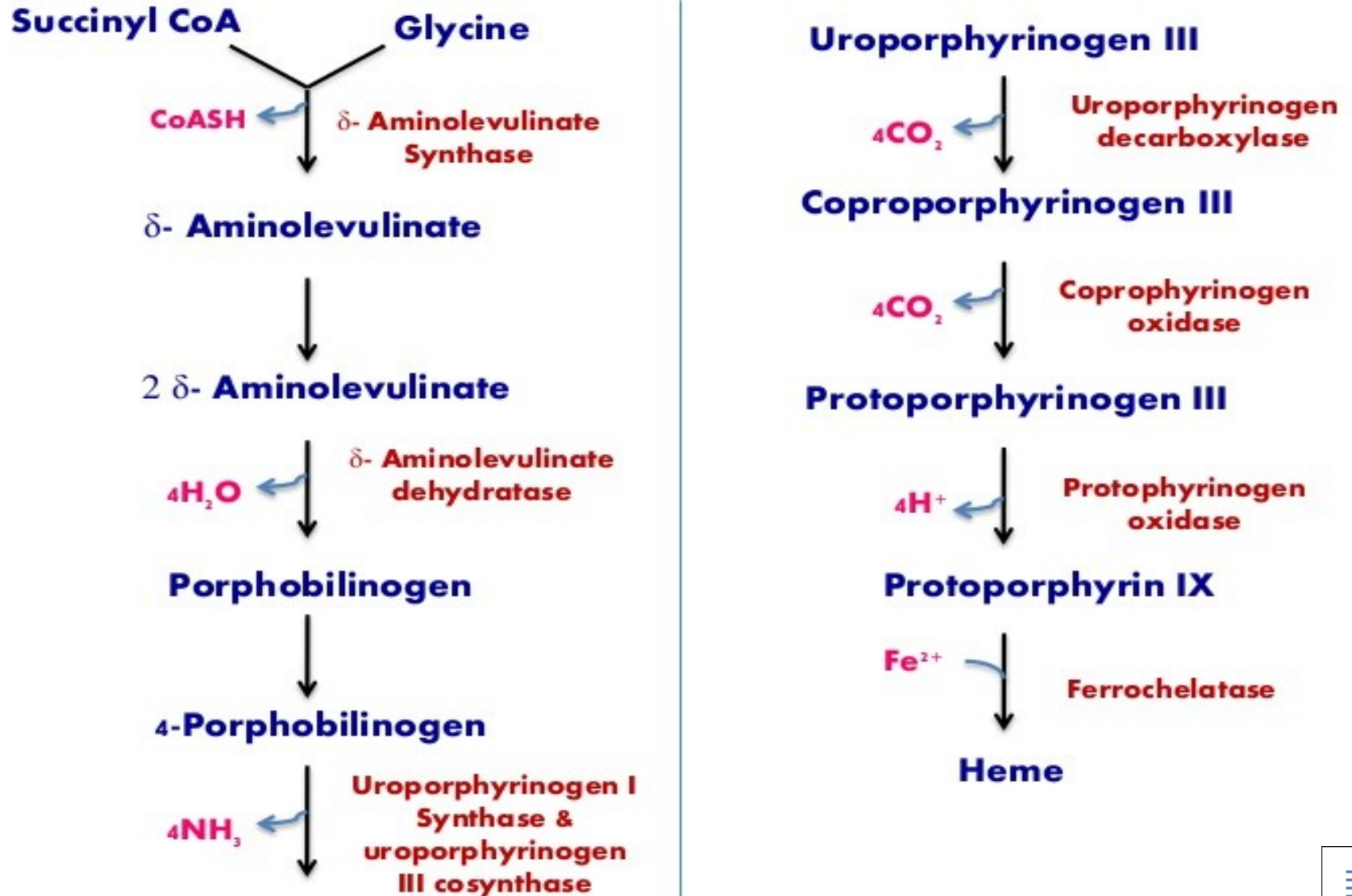
Clinical Disorders of Heme Synthesis

What is Porphyria

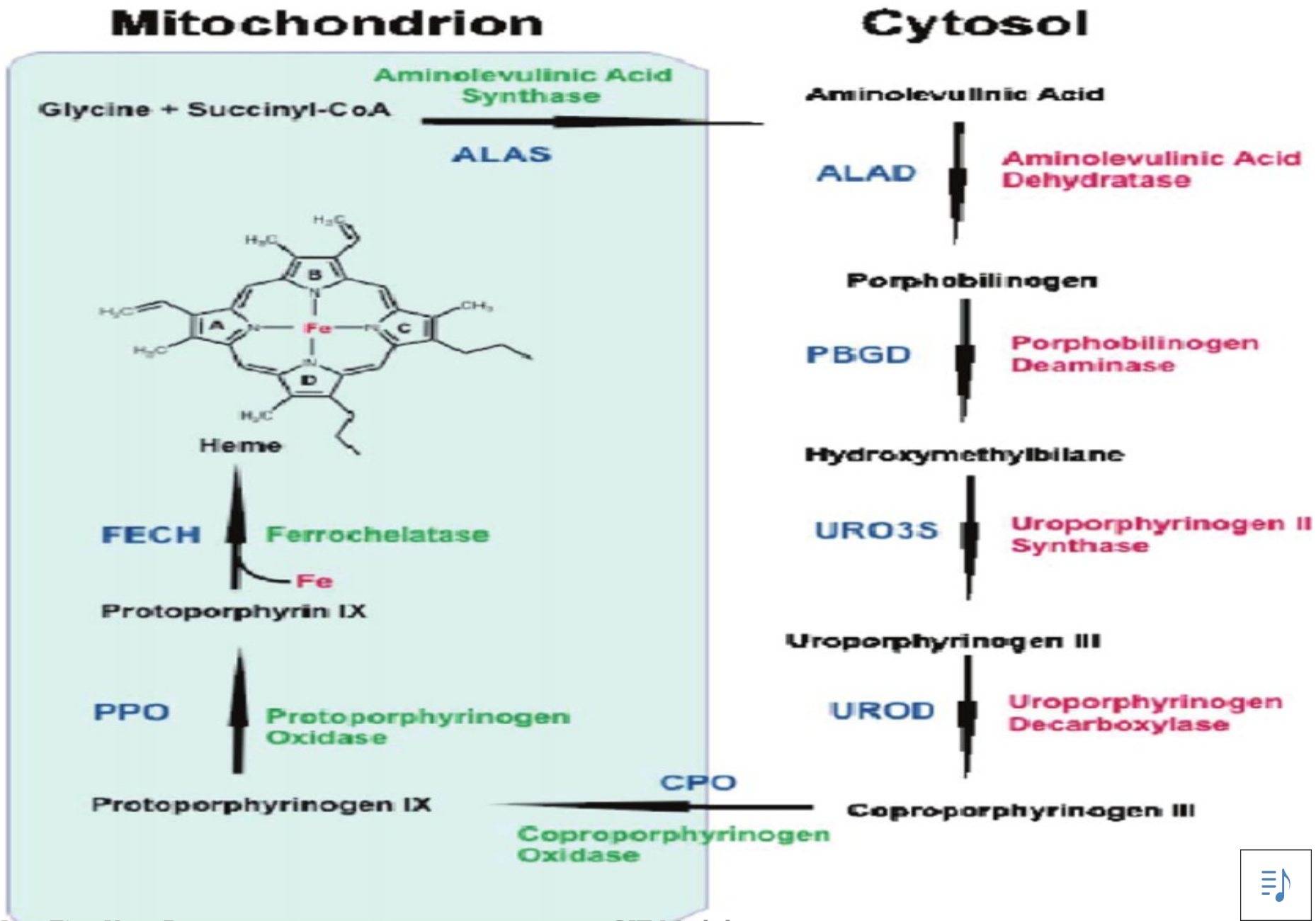


Overall reactions of heme biosynthesis

Synthesis of heme



Overall reactions of heme biosynthesis



A stethoscope with a black tube and silver chest piece is resting on a human torso. The background is a warm, golden-brown color with a subtle pattern of overlapping circles. The title text is overlaid on the right side of the image.

Clinical Disorders of Heme Synthesis



1. Lead Poisoning

Due to high exposure to: Lead paints, batteries and water lead pipes.

:Lead inhibits 2 enzymes

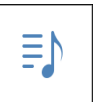
ALA dehydratase & Ferrochelatase



ALA and protoporphyrin accumulate in urine



Elevation in ALA and anemia



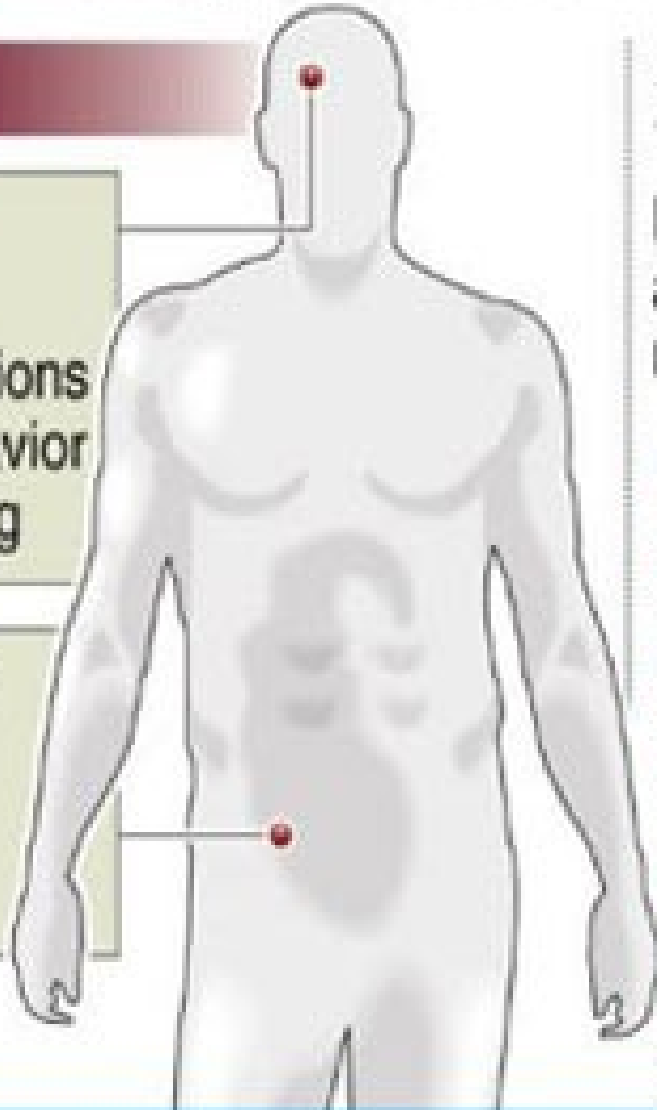
Lead poisoning

Lead buildup in the body causes serious health problems

Symptoms

- Headaches
- Irritability
- Reduced sensations
- Aggressive behavior
- Difficulty sleeping

- Abdominal pain
- Poor appetite
- Constipation
- Anemia



Additional complications for children:

Lead is more harmful to children as it can affect developing nerves and brains

- ▶ Loss of developmental skills
- ▶ Behavior, attention problems
- ▶ Hearing loss
- ▶ Kidney damage
- ▶ Reduced IQ
- ▶ Slowed body growth



What is Porphyria

Porphyria

vampire disease



2. Porphyrrias

Porphyrias are rare, inherited (or occasionally acquired in lead poisoning) defects in heme synthesis, resulting in the accumulation and increased excretion of porphyrins or porphyrin precursors

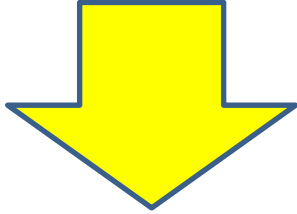


2. Porphyrrias

**Porphyria” refers to
the red-blue color
caused by pigment-
like
porphyrins in the
urine of patients
with defects in heme
synthesis**



**The porphyrias are classified
as**



1-Erythropoietic



Hepatic-2

**Depending on whether the enzyme
deficiency occurs in the erythropoietic
cells of the bone marrow or in the liver**



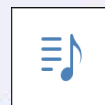
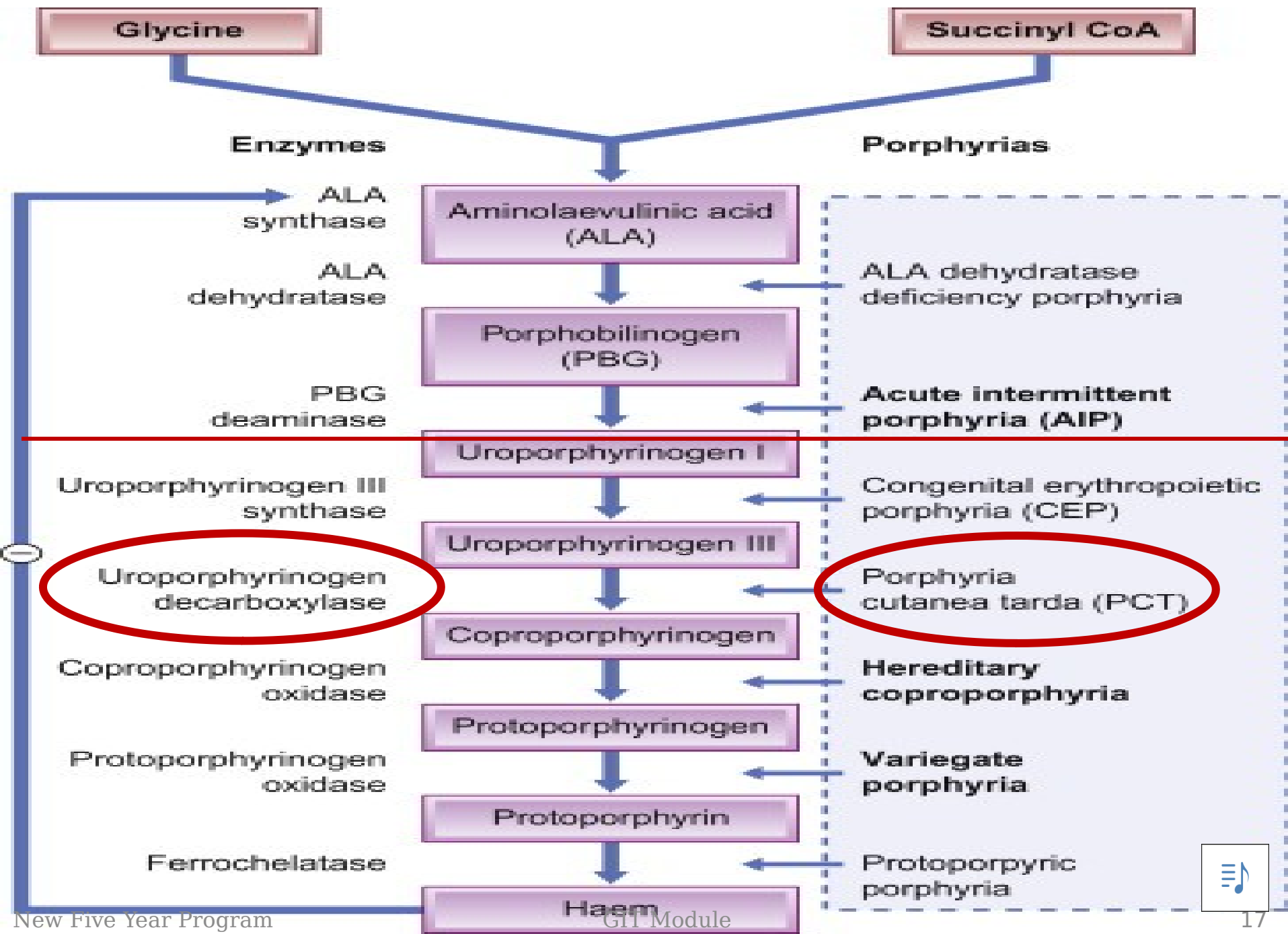
Clinical :manifestations

If the enzyme defect
prior to the formation of
porphyrinogens
(tetrapyrroles)

Abdominal and
neuropsychiatric signs

If the enzyme defects
after the formation
porphyrinogens

Photosensitivity
skin itches, burns and)
pruritus on exposure to
(visible light





Note: Photosensitivity is a result of the **oxidation** of colorless **porphyrinogens** to colored **porphyrins**, that participate in the formation of **superoxide radicals** from oxygen

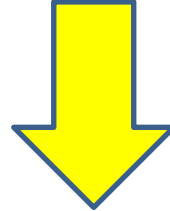
These reactive oxygen species can oxidatively **damage membranes** and cause the release of destructive enzymes from

Lysosomes

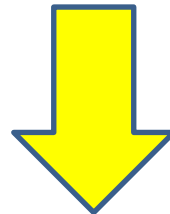


Clinical manifestations

**One common feature of the porphyrias is a
decreased synthesis of heme**



**Increase in the synthesis of ALAS1
(derepression)**



**Increased synthesis and accumulation of
toxic intermediates that occur prior to the
genetic block**





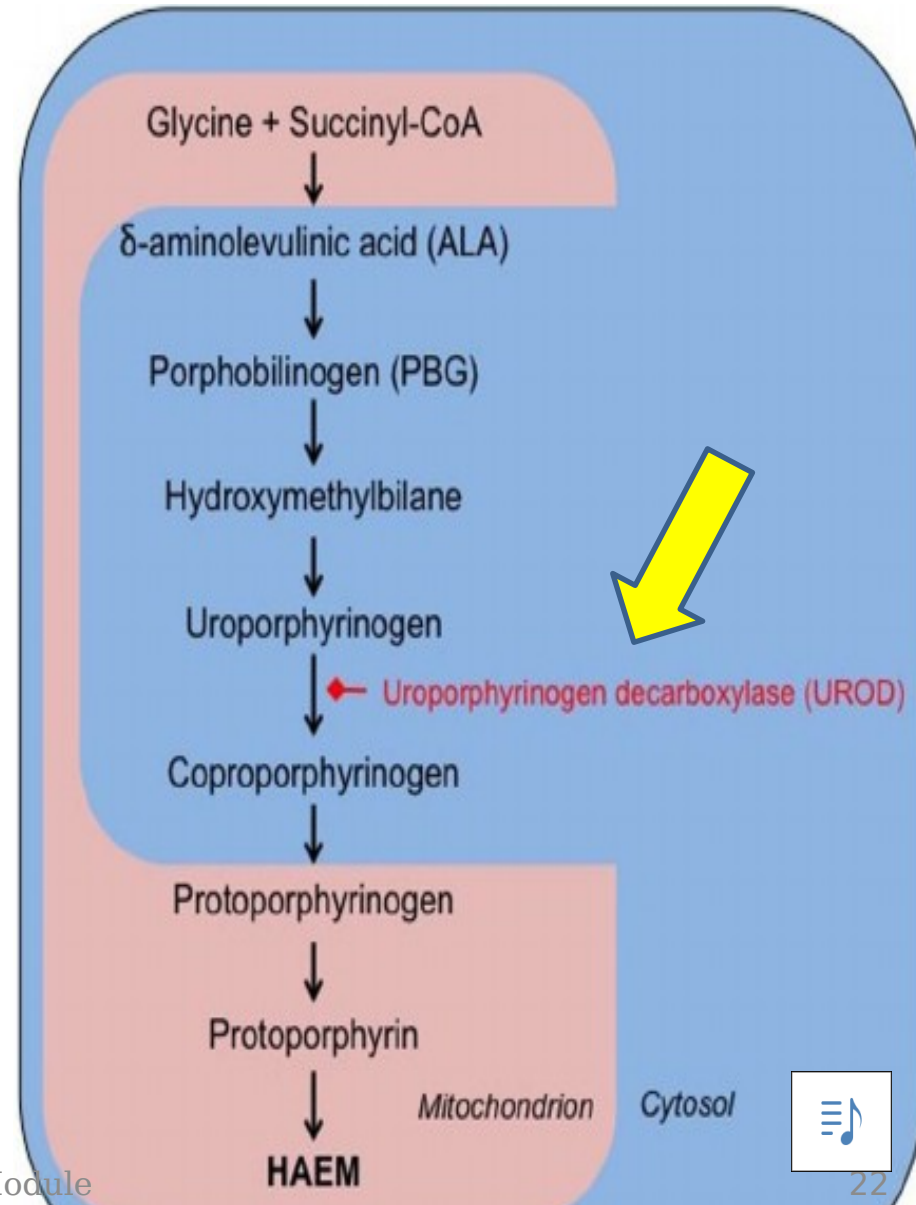
Porphyria Cutanea Tarda



Porphyria cutanea tarda

It is the **most common** porphyria

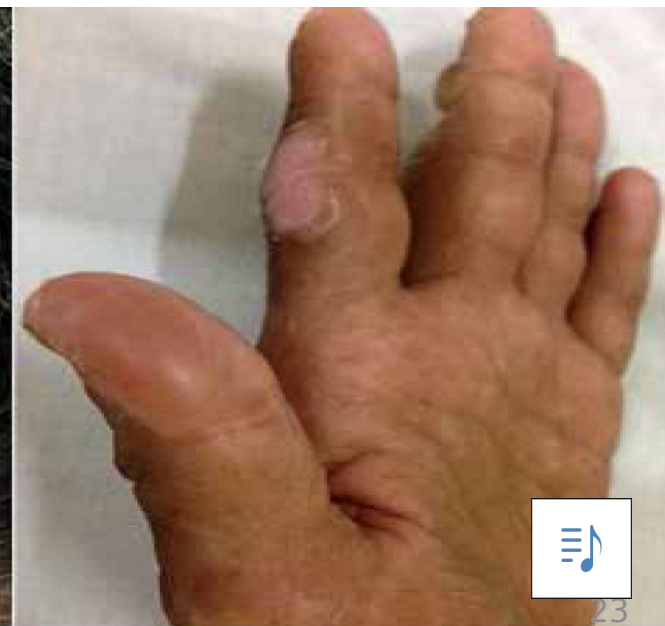
It occurs due to **deficiency in uroporphyrinogen decarboxylase enzyme**

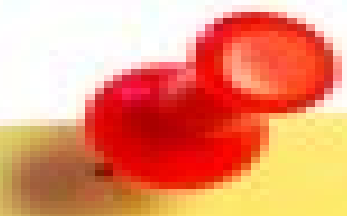


Porphyria cutanea tarda

Clinical **onset** is during the **fourth** or **fifth** decade of life

Porphyrin accumulation leads to **cutaneous symptoms** and **red** to **brown urine** in natural light





Note: Symptoms of the acute hepatic porphyrias often **precipitated** by drugs that cause **induction of cytochrome P450** e.g. **.steroids , alcohol, Phenobarbital**
These drugs are contraindicated
.for porphyria patients

?WHY



?WHY

Intake of **drugs** as barbiturates or ethanol



Induce the synthesis of the heme containing
cytochrome P450 required for their metabolism



Decrease heme level in liver cells



Increase synthesis of **ALAS**



More increase of **porphyrins** & exacerbation of
symptoms



Treatment

**No curable treatment,
only medical support during
acute attacks and
symptomatic treatment for pain
and vomiting**



Treatment

1. Intravenous injection of **hemin** and **glucose** to decreases the synthesis of **ALAS1**.
2. **Avoidance** of precipitating **drugs**.
3. **Protection** from **sunlight**.
4. **Anti-oxidants:** vitamin A (**β -carotene**) & **Vit E** in cases of **photosensitivity**.



MCQ

**Biochemical basis of precipitation -1
:of porphyria by barbiturates is**

- A. Repression of ALA synthase**
- ☒ B. Derepression of ALA synthase**
- C. Rerepression of ALA synthase**
- D. MiRNA mediated**



MCQ

**Most common porphyria is due to -2
:deficiency of**

A. PBG deaminase

☒ B. Uroporphyrinogen decarboxylase

C. Ferrocheletase

D. Coproporphyrinogen oxidase

E. ALA synthase



Summary

- **Lead poisoning is due to high exposure to:
Lead paints, batteries and water lead pipes.**
- **“Porphyria” refers to the red-blue color caused by pigment-like porphyrins in the urine of patients with defects in heme synthesis**
- **Porphyria cutanea tarda occurs due to deficiency in uroporphyrinogen decarboxylase enzyme**

Thank
you

Marwa Al

